REMARKS

In the instant Action, Claims 1-28 are listed as pending, Claims 14-28 are listed as withdrawn from consideration for being drawn to the nonelected method of use inventions (but which are subject to rejoinder upon allowance of product claims), and Claims 1-13 are listed as rejected.

In reply to the instant Action, Applicant has canceled Claims 1 and 2, and has amended claims 3, 14, 15, 18-21, and 24 to incorporate the limitations of the now canceled Claim 1 and otherwise to indicate proper dependency. No new matter has been introduced by said amendments, which are submitted without waiver or prejudice to Applicant's ability to pursue any subject matter canceled thereby.

- ***Information Disclosure Statement***

Applicant gratefully notes that the Examiner has acknowledged the information disclosure statements, received 8/29/05 and 10/13/06.

- ***Claim Rejections – 35 U.S.C. §102***

Although these rejections under 35 U.S.C. §102 appear as the last item in the instant Action, Applicant will address this first in view of Applicant's belief that this rejection resulted from the Examiner's erroneous understanding of law of anticipation under §102, which requires "sameness", either expressly or inherently, under the anticipation jurisprudence as clearly established by case law.

It is axiomatic that anticipation of a claim under §102 can be found only if the prior art reference discloses every element of the claim. See *In re King*, 801 F.2d 1324, 1326, 231 USPQ 136, 138 (Fed. Cir. 1986) and *Lindemann Maschinenfabrik GMBH v. American Hoist & Derrick Co.*, 730 F.2d 1452, 1458, 221 USPQ 481, 485 (Fed. Cir. 1984). In rejecting claims under 35 U.S.C. §102, a single prior art reference that discloses, either expressly or inherently, each limitation of a claim invalidates that claim by anticipation. *Perricone v. Medicis Pharmaceutical Corp.*, 432 F.3d 1368, 1375-76, 77 USPQ2d 1321, 1325-26 (Fed. Cir. 2005), citing *Minn. Mining & Mfg. Co. v. Johnson & Johnson Orthopedics, Inc.*, 976 F.2d 1559, 1565, 24 USPQ2d 1321, 1326 (Fed. Cir. 1992). Anticipation of a patent claim

requires a finding that the claim at issue "reads on" a prior art refference. *Atlas Powder Co. v. IRECO, Inc.*, 190 F.3d 1342, 1346, 51 USPQ2d 1943, 1945 (Fed. Cir. 1999) ("In other words, if granting patent protection on the disputed claim would allow the patentee to exclude the public from practicing the prior art, then that claim is anticipated, regardless of whether it also covers subject matter not in the prior art.") (internal citations omitted).

At pages 7-8 of the instant Action, the Examiner states:

> The instant invention is drawn to a compound according to the formula: $[A5C^{31}]hPYY(3\text{-}36)NH_2$, (SEQ ID NO:3).
>
> Quay et al. [USPN 7,157,426] discloses a PYY composition comprising the amino acid sequence of SEQ ID NO:2, a 99% match to instant SEQ ID NO:3. See, for example, SEQ ID NO:2 and claim 1.

SEQ ID NO:2 from Quay et al. is reproduced below:

<210> SEQ ID NO 2
<211> LENGTH: 34
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 2

```
Ile Lys Pro Glu Ala Pro Gly Glu Asp Ala Ser Pro Glu Glu Leu Asn
 1               5                  10                  15

Arg Tyr Tyr Ala Ser Leu Arg His Tyr Leu Asn Leu Val Thr Arg Gln
            20                  25                  30

Arg Tyr
```

It is immediately apparent that SEQ ID NO:2 from Quay et al. is that of ***native*** "Homo sapience" sequence. Column 11 of Quay et al. makes this fact clear, as reproduced below:

> As used herein, "PYY" refers to PYY(1–36) in native-sequence or in variant form, as well as derivatives, fragments, and analogs of PYY from any source, whether natural, synthetic, or recombinant. The PYY must be comprised at least the last 15 amino acid residues or analogoues thereof of the PYY sequence,PYY(22–36) (SEQ ID NO: 3). Other PYY peptides, which may be used are PYY(1–36) (SEQ ID NO: 1) PYY(3–36) SEQ ID NO: 2) PYY(4–36)

SEQ ID NO:3 for $[A5C^{31}]hPYY(3\text{-}36)NH_2$ is reproduced below:

<210> 3
<211> 34
<212> PRT
<213> artificial

<220>
<223> C-terminal amidation

<220>
<221> MISC_FEATURE
<222> (29)..(29)
<223> Xaa is 1-amino-1-cyclopentanecarboxylic acid

<400> 3

Ile Lys Pro Glu Ala Pro Gly Glu Asp Ala Ser Pro Glu Glu Leu Asn
1 5 10 15

Arg Tyr Tyr Ala Ser Leu Arg His Tyr Leu Asn Leu Xaa Thr Arg Gln
20 25 30

Arg Tyr

It is immediately apparent that SEQ ID NO:3 for [A5C^{31}]hPYY(3-36)NH_2 is "artificial" sequence having a substitution at the 31st position with an artificial amino acid, *i.e.* "Xaa is 1-amino-1-cyclopentanecarboxylic acid".

It is remarkable to propose, as the Examiner does in the instant Action, that a ***native*** sequence somehow anticipates under §102 an ***artificial*** sequence having ***different*** sequence than the native sequence. The Examiner in essence proposes that the fact that the claimed compound [A5C^{31}]hPYY(3-36)NH_2 has the artificial amino acid residue A5C, *i.e.*, 1-amino-1-cyclopentanecarboxylic acid, at position 31 whereas the native sequence has the naturally-occurring valine (*i.e.*, Val) is not relevant to the anticipation analysis under §102. The Examiner's remark that "a 99% match" between the claimed compound and the native sequence is sufficient to establish a prima facie case of anticipation cannot stand in view of the clearly established law of anticipation requiring that a single art reference must disclose each limitation of a claim. Applicant respectfully traverses this rejection and asserts that "a 99% match" cannot support a finding that the claim having A5C substitution at a particular position "reads on" the native sequence which by definition does not have this artificial substitution.

In view of the foregoing discussion, Applicant respectfully requests reconsideration and withdrawal of this rejection.

- ***Claim Rejections – 35 U.S.C. §112, first paragraph (Written Description)***

The Examiner has rejected Claims 1-7 and 13 under 35 U.S.C. §112, first paragraph, as failing to comply with the written description requirement.

In the instant Action, the Examiner directs Applicant to the Guidelines for the Examination of Patent Applications Under the 35 U.S.C., para. 1, "Written Description" Requirement (hereinafter referred to as the "Guidelines"). After having studied the Guidelines, Applicant is under the impression that the Examiner has misunderstood the nature of the claimed invention and in at least some ways misapplied the law of written description as set forth in the Guidelines.

But first, Applicant would again like to point out that if the Examiner is persuaded by Applicant's argument above with respect to the anticipation rejections under 35 U.S.C. §102 – as an artificially substituted sequence is different from a native sequence and cannot be "anticipated" under §102 as the case law clearly establishes – then at least Claims 8-12 should be allowed in the next Action.

In any event, without in any way acquiescing to the Examiner's reasoning in the instant Action, but solely in order to place this application in a condition for allowance, Applicant's has canceled the *broadest* Claims 1 and 2, and has amended Claim 3 to incorporate the remaining limitations of Claim 1. For instance, Claim 3, as amended, includes the following *proviso* clauses (underlining is to show the added text):

provided that when R^2 is (C_1-C_{30})acyl, aryl(C_1-C_{30})acyl, substituted (C_2-C_{30})acyl, or substituted aryl(C_1-C_{30})acyl, R^3 is -H, (C_1-C_{30})alkyl, (C_1-C_{30})heteroalkyl, (C_2-C_{30})alkenyl, (C_2-C_{30})alkynyl, aryl(C_1-C_{30})alkyl, substituted (C_1-C_{30})alkyl, substituted (C_1-C_{30})heteroalkyl, substituted (C_2-C_{30})alkenyl, substituted (C_2-C_{30})alkynyl, or substituted aryl(C_1-C_{30})alkyl;

R^4 and R^5 each is, independently for each occurrence, selected from the group consisting of -H, (C_1-C_{40})alkyl, (C_2-C_{40})acyl, (C_1-C_{30})alkylsulfonyl, and -C(NH)NH_2,

provided that when R^4 is (C_1-C_{40})acyl, (C_1-C_{30})alkylsulfonyl, or -C(NH)NH_2, then R^5 is -H or (C_1-C_{40})alkyl;

n is, independently for each occurrence, 1, 2, 3, 4 or 5; and

X^1, X^2, X^3, X^4, and X^5 each is, independently for each occurrence, selected from the group consisting of -H, -F, -Cl, -Br, -I, (C_1-C_{10})alkyl, substituted (C_1-C_{10})alkyl, aryl, substituted aryl, -OH, $-NH_2$, $-NO_2$, and -CN;

provided that:

(a) said peptide comprises at least one amino acid selected from the group consisting of:

(i) Acc at A^3, A^6, A^7, A^9, A^{10}, A^{11}, A^{12}, A^{15}, A^{16}, A^{17}, A^{18}, A^{20}, A^{21}, A^{22}, A^{24}, A^{27}, A^{28}, A^{29}, A^{30}, A^{31}, A^{32}, or A^{34};

(ii) Act at A^3, A^7, A^{12}, A^{13}, A^{22}, A^{23}, or A^{32};

(iii) Apc at A^4, A^7, A^{12}, A^{19}, A^{22}, A^{25}, A^{26}, A^{33}, A^{34}, A^{35}, or A^{36};

(iv) Aib at A^6, A^7, A^9, A^{10}, A^{11}, A^{12}, A^{13}, A^{15}, A^{16}, A^{18}, A^{22}, A^{29}, or A^{32};

(v) Thz, Dmt, Dhp, Ktp, or Tic at A^5, A^8, or A^{14};

(vi) (3,4,5-F)Phe or (2,3,4,5,6-F)Phe at A^{20}, A^{21}, A^{26}, A^{27}, or A^{36};

(vii) 2Fua at A^{20}, A^{21}, A^{26}, or A^{27};

(viii) Taz at A^{20}, A^{21}, or A^{26}; and

(ix) 2Pal, 3Pal, 4Pal, 2Thi or 3Thi at A^{26};

(b) if A^3 - A^{21} are deleted and (i) A^{22} is Aib or (ii) A^{36} is (3,4,5-F)Phe or (2,3,4,5,6-F)Phe, then A^{27} is not 2Thi, Trp, 2Nal, or (X^1,X^2,X^3,X^4,X^5)Phe, wherein X^1 is *p*-chloro and X^2, X^3, X^4 and X^5 each is -H; and

(c) each amino acid A^m of formula (I) may be deleted only if A^{m-1} is deleted, wherein m is an integer ranging in value from 4 - 26, inclusive;

It should be noted that the above reproduced *proviso* clause (a) ensures that the claimed compound does *not* read on a ***native*** sequence including that of Quay et al. cited by the Examiner, and discussed above in connection with the anticipation rejection under §102. It should also be noted that Claim 3, as amended, greatly limits the definitions of A^3 to A^{36}, as compared to the corresponding definitions in Claim 1, now canceled. As such, Applicant respectfully traverses the Examiner's remarks at page 4 of the instant Action that "the specification fails to provide sufficient descriptive information, such as definitive structural or functional features, or critical conserved regions, of the genus and subgenera of proteins to be used in the claimed composition."

To further illustrate Applicant's point in this regard, the original Claim 6 depends on the original Claims 1-5 and incorporates all of the specific structural limitations of said intervening claims, including the *proviso* claims (a)-(c) which require that the claimed

compound include at least one or two non-naturally occurring amino acid substitutions. That is, Claim 5 is directly supportive of, and closely tailored to, all of the specific compounds of Claim 8, and it should be noted that Claim 8 directly depends on Claim 7, and the Examiner does not object to Claim 8 for lacking adequate written description. In this regard, Applicant respectfully asserts that the Examiner's assertion at page 4 of the instant Action is oversimplification and fails to take into account all of the specific structural features defined for each of the amino acid residue positions A^3 to A^{36} and other specific structural features that clearly distinguish the claimed compound as being novel and nonobvious, such as the *proviso* clauses (a)-(c):

> One of skill in the art would not recognize from the disclosure that the applicant was in possession of the genus of which comprises the compound of the formula I: (R2,R3) A3-A4-A5-A6-A7-A8-A9-A10-A11-A12-A13-A14-A15-A16-A17-A18-A19-A20-A21-A22-A23-A24-A25-A26-A27-A28-A29-A30-A31-A32-A33-A34-A35-A36-R1.

In fact, the Guidelines require that "The examiner should evaluate **each claim** to determine if sufficient structures, acts, or functions are recited to make clear the scope and meaning of the claim, including the weight to be given the preamble." (emphasis added). At page 5 of the instant Action, the Examiner states that "All other claims depend directly or indirectly from the rejected claim [1] and are, therefore, also rejected under 35 USC 112, first paragraph for the reasons set forth above." From this, it is clear that the Examiner only examined the original Claim 1 for compliance with 35 USC §112, first paragraph, and failed to examine the subgenus formulas recited in the original Claims 2-7. Applicant further respectfully points out that subgenus formulas of the original Claims 2-7 are each narrow in scope of their specific structural limitations than the preceding claims on which they depend either directly or indirectly. As illustrated above, by the time the original Claim 6 is reached, only the specific structural features for the definitions of A^3 to A^{36} corresponding to those specific compounds of the original Claim 8 remain in the claim. If the Examiner does not object to Claim 8, then the original Claim 6 is most likely compliant with the written description requirement of §112, first paragraph, if the Examiner had in fact examined it as required by the Guidelines.

In this regard, the Guidelines further provide that "A description as filed is presumed to be adequate, unless or until sufficient evidence or reasoning to the contrary has been presented by the examiner to rebut the presumption. See, e.g., *In re Marzocchi*, 439 F.2d 220, 224, 169 USPQ 367, 370 (CCPA)." As noted above, Applicant believes that the Examiner simply concluded that the original Claim 1 is not adequately described and failed to examine the original Claims 2-7 as depending directly or indirectly from the rejected original Claim 1. As such, if the Examiner still finds that Claim 3, as amended, as well as the increasingly narrower Claims 4-7 are still not adequately described under §112, first paragraph, Applicant respectfully requests that the Examiner make the next Action *non-final.*

- ***Claim Rejections – 35 U.S.C. §112, first paragraph (Enablement)***

The Examiner has rejected Claims 1-7 and 13 under 35 U.S.C. §112, first paragraph, as failing to comply with the enablement requirement.

But first, Applicant would again like to point out that if the Examiner is persuaded by Applicant's argument above with respect to the anticipation rejections under 35 U.S.C. §102 – as an artificially substituted sequence is different from a native sequence and cannot be "anticipated" under §102 as the case law clearly establishes – then at least Claims 8-12 should be allowed in the next Action. Further, it would appear that the Examiner simply concluded that the original Claim 1 is not adequately enabled as being overbroad and failed to examine the original Claims 2-7 as depending directly or indirectly from the rejected original Claim 1. (See page 7 of the instant Action: "All other claims depend directly or indirectly from rejected claims and are, therefore, also rejected under 35 U.S.C. 112, first paragraph") As such, if the Examiner still finds that Claim 3, as amended, as well as the increasingly narrower Claims 4-7 are still not adequately enabled under §112, first paragraph, Applicant respectfully requests that the Examiner make the next Action *non-final.*

As discussed above, without in any way acquiescing to the Examiner's reasoning in the instant Action, but solely in order to place this application in a condition for allowance, Applicant's has canceled the *broadest* Claims 1 and 2, and has amended Claim 3 to incorporate the remaining limitations of Claim 1.

At pages 6-7 of the instant Action, the Examiner has expressly acknowledged as follows:

> The breadth of the claims is excessive with regard to claiming a compound of formula I. Applicant has only provided guidance for the use of SEQ ID NO:3, 5, 8, 10, 13 and 64.
>
> Applicant's working examples of SEQ ID NO: 1-30 in example 29 on page 38 of the instant specification shows a binding to the Y2 receptor, but only speaks to possible antisecretory effects and the effects on intestinal water and sodium absorption. The absence of working examples dealing with the practice of the invention, an effective amount of any of the peptides, the administration of the compound, is lacking.

On the one hand, the Examiner says that Applicant has provided sufficient guidance for the use of SEQ ID NO:3, 5, 8, 10, 13 and 64; on the other hand, the Examiner says that the absence of working examples dealing with the practice of the invention, an effective amount of any of the peptides, and the administration of the compound, makes all claims depending directly or indirectly from the original Claim 1 not enabled. In other words, one would logically infer from the Examiner's rationale that there is adequate description of an effective amount and the administration of SEQ ID NO:3, 5, 8, 10, 13 and 64, but not for any other claimed compounds. Applicant would simply submit that if the Examiner has found that there is adequate description of an effective amount and the administration of SEQ ID NO:3, 5, 8, 10, 13 and 64, but not for any other claimed compounds, then there is adequate description of an effective amount and the administration of all claimed compounds because such details are provided in general terms as a medical chemist or a reasonably skilled physician would be enabled to determine such information on the basis of each individual.

Another apparent inconsistency in the above quoted statement is that the Examiner considers *in vitro* binding data, *i.e.*, "a binding to the Y2 receptor", to be insufficient indicia of enablement in the absence of *in vivo* data such as "possible antisecretory effects and the effects on intestinal water and sodium absorption." MPEP §2164.02 provides that "An *in vitro* **or** *in vivo* animal model example in the specification, in effect, constitutes a 'working example' if that example 'correlates' with a disclosed or claimed **method** invention." It should be noted that, as noted above, the original Claims 14-28 drawn to the nonelected method of use invention are withdrawn from consideration, and only the "compound" claims 1-13 are being examined on their merits.

With respect to "Applicant's working examples of SEQ ID NO: 1-30 in example 29 on page 38 of the instant specification", the Examiner has already acknowledged that there is sufficient experimental support in the specification as filed. With respect to the claimed "compounds" for which Applicant has not submitted experimental data, it is evident that it would not require "undue experimentation" for a skilled medicinal chemist to follow the same procedure as outlined in the instant specification and based on the readily available prior art knowledge to obtain similar experimental data. In the absence of any indication in the instant Action that the disclosed assay would entail undue experimentation, Applicant respectfully submits that all of the claimed compounds are sufficiently enabled. That is, there is no objective indication that the skilled artisan would be unable to follow the disclosed assay without undue experimentation.

At page 7 of the instant Action, the Examiner states "it is apparent that there is undue experimentation because of a variability in prediction of outcome that is not addressed by the present application." Again, the Examiner assumes that a skilled artisan would be left to predict the claimed compound's activity – again, only those claims drawn to compounds are being examined on the merits – based on some structure/activity relationship, even when Applicant has provided enabling disclosure to synthesize and test any of the claimed compounds. Further, a skilled physician can determine the exact dosage and route of administration depending on each patient determined to be in need of such treatment. By providing sufficiently clear and easy to follow disclosure to make and use the claimed compounds, a skilled artisan is not left to predict pharmacological efficacy merely by studying the structure of a compound, but rather, he/she is presumed to follow the disclosed synthetic and assay descriptions to make and use the claimed invention.

At page 7 of the instant Action, the Examiner states "Absent factual data to the contrary, the amount and level of experimentation needed is undue to practice the invention as claimed." Again, only claims drawn to "compounds" are being examined on the merits. Further, Applicant's undersigned attorney is not aware of such *per se* requirement, i.e., requirement that Applicant include experimental data at the time of filing, under U.S. law. In any event, Applicant has included sufficient *in vitro* binding data in the specification at the time filing to demonstrate that the claimed compounds are at least promising candidates for further research and development which may undergo drug application process before the

U.S. Food and Drug Administration. It should be noted that different "enablement" standards apply before the U.S.P.T.O. and the U.S. Food and Drug Administration. For one thing, *in vivo* pharmacological experimental data is certainly not required to satisfy the enablement requirement under §112, first paragraph, as the Examiner seems to presume.

For the foregoing reasons, Applicant respectfully requests reconsideration and withdrawal of the rejections under §112, first paragraph.

In conclusion, reconsideration of the instant Action, entry of the requested amendments, grant of the requested rejoinder and examination on the merits of Claims 14-28 drawn to the nonelected method of use invention, and allowance of all pending claims are respectfully requested.

Prompt and favorable action is solicited.

Examiner Telleris invited to telephone Applicant's undersigned if deemed necessary to facilitate prosecution of this application.

Respectfully submitted,

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